Office de la Propriété Intellectuelle du Canada
Un organisme d'Industrie Canada

Canadian Intellectual Property Office
An agency of Industry Canada

CA 2393614 C 2003/09/30

(11)(21) 2 393 614

SECTION 8 CORRECTION
SEE CERTIFICATE
CORRECTION - ARTICLE 8
VOIR CERTIFICAT

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(22) Date de dépôt/Filing Date: 2002/07/19

(41) Mise à la disp. pub./Open to Public Insp.: 2002/10/28

(45) Date de délivrance/Issue Date: 2003/09/30

(51) Cl.Int.^{7}/Int.Cl.^{7} A61K 31/7048, A61P 31/04

(72) Inventeurs/Inventors:
SALEKI-GERHARDT, AZITA, US;
RAFELDT, RICK, US

(73) Propriétaire/Owner:
ABBOTT LABORATORIES, US

(74) Agent: TORYS LLP

(54) Titre : COMPOSITIONS ANTIBACTERIENNES DE CLARITHROMYCINE ET PROCESSUS DE PREPARATION CONNEXE

(54) Title: ANTIBACTERIAL CLARITHROMYCIN COMPOSITIONS AND PROCESSES FOR MAKING THE SAME

(57) Abrégé/Abstract:
Abridged clarithromycin antibacterial compositions and methods for making the same are disclosed

Office de la propriété intellectuelle du Canada
Un organisme d'Industrie Canada

Canadian Intellectual Property Office
An Agency of Industry Canada

Bureau canadien des brevets
Certificat de correction

Canadian Patent Office
Certificate of Correction

Canadian Patent No. 2,393,614
Granted: September 30, 2003

Les corrections suivantes sont faites en raison de l'article 8 de la *Loi sur les brevets* et le document doit être lu tel que corrigé.

The following corrections are made pursuant to section 8 of the *Patent Act* and the document should read as corrected.

In the Patent Grant:

1. In the disclosure page 7 has been replaced with a new page to realign table found at lines 8 to 12.

Agent certificateur / Certifying Officer

January 13, 2004

Date

Canada

(CIPO 25)
01/04/03

OPIC CIPO

ABSTRACT

Abridged clarithromycin antibacterial compositions and methods for making the same are disclosed

ANTIBACTERIAL CLARITHROMYCIN COMPOSITIONS AND PROCESSES FOR MAKING THE SAME

FIELD OF THE INVENTION

This invention is directed to abridged clarithromycin antibacterial compositions and methods for making the same.

BACKGROUND OF THE INVENTION

Clarithromycin is employed in the manufacture of commercially-available antibiotic compositions for human administration. For example, an orally-administered antibacterial composition of clarithromycin in tablet form consists essentially of clarithromycin and a number of excipients which, in toto, control the bioavailability of the antibiotic.

The removal of one or more of these excipients from the composition to provide an abridged antibacterial composition of clarithromycin with substantially similar antibiotic activity of the clarithromycin would provide a more streamlined, less costly avenue toward commercial-availability of the drug. In addition, an abridged antibacterial composition of clarithromycin, if smaller in size or offering other advantages, would be better tolerated by patients. Therefore, there is an existing need in the formulations art for an abridged antibacterial composition of clarithromycin.

SUMMARY OF THE INVENTION

The first embodiment of this invention, therefore, is directed to an abridged antibacterial clarithromycin composition consisting essentially of clarithromycin, water, an intra-granular excipient, and an extra-granular excipient, in which the granular excipient consists essentially of povidone, sodium croscarmellose, and microcrystalline celluose, and the extra-granular excipient consists essentially of sodium croscarmellose, microcrystalline celluose, colloidal silicon dioxide, and impalpable magnesium stearate powder.

A second embodiment of this invention is directed to a process for making an abridged antibacterial clarithromycin composition,

the process comprising the steps of:

(a) granulating a mixture consisting essentially of povidone, clarithromycin, sodium croscarmellose, microcrystalline celluose, and water to provide a wet intra-granular excipient;

(b) drying the wet intra-granular excipient to provide a dry intra-granular excipient; and

(c) mixing the dry intra-granular excipient and an extra-granular excipient, the extra-granular excipient consisting essentially of sodium croscarmellose, microcrystalline celluose, colloidal silicon dioxide, and impalpable magnesium stearate powder.

A third embodiment of this invention is directed to a medicament consisting essentially of an abridged antibacterial clarithromycin composition.

A fourth embodiment of this invention is directed to use of an abridged antibacterial clarithromycin composition in the preparation of a medicament, the medicament being useful for prophylaxis or treatment of bacterial infections in a mammal.

DETAILED DESCRIPTION OF THE INVENTION

The currently commercially-available, non-abridged clarithromycin composition consists essentially of the following components: clarithromycin, colloidal silicon dioxide, D&C yellow dye No. 10, extra-granular sodium croscarmellose, extra-granular microcrystalline celluose (Avicel® PH-102), intra-granular sodium croscarmellose, intra-granular microcrystalline celluose (Avicel® PH-101), magnesium stearate powder, povidone, pre-gelatinized starch, 200 proof alcohol, stearic acid, talc, and water.

This invention is directed to abridged antibacterial clarithromycin compositions, hereinafter referred to as "abridged compositions," which contain any amount of clarithromycin and from which at least one of the aforementioned components have been omitted.

In a preferred first embodiment, the abridged compositions contain the same amount of clarithromycin which is currently available in non-abridged adult and pediatric formulations, such as, for example, 250 mg of clarithromycin or 500 mg of clarithromycin for the adult formulations and aqueous solutions comprising 125 mg per 5 mL or 250 mg per 5 mL of clarithromycin for the pediatric formulations.

In still another preferred first embodiment, the 200 proof alcohol, stearic acid, and talc have been omitted from the abridged compositions.

In still yet another preferred first embodiment, the 200 proof alcohol, stearic acid, talc pre-gelatinized starch and D&C yellow dye No. 10 have been omitted from the abridged compositions.

In still even yet another preferred first embodiment, the microcrystalline celluose of the intra-granular excipient comprises Avicel® PH-101.

In still even yet another preferred first embodiment, the microcrystalline celluose of the extra-granular excipient comprises Avicel® PH-102.

In still even yet another preferred first embodiment, the colloidal silicon dioxide of the extra-granular excipient comprises Cab-O-Sil™ M-5.

In still even yet another preferred first embodiment, the abridged compositions contain 4.0% to 5.9% by weight povidone, 3.0% to 6.8% by weight intra-granular sodium croscarmellose, 2.2% to 7.5% by weight intra-granular microcrystalline celluose, 3.0% to 6.8% by weight extra-granular sodium croscarmellose, 6.9% to 15.9% by weight extra-granular microcrystalline celluose, 0.5% to 0.8% by weight, colloidal silicon dioxide, and 1.5% to 2.5% by weight magnesium stearate powder.

In a more preferred first embodiment, the abridged compositions contain 4.9% by weight povidone, 4.9% by weight intra-granular sodium croscarmellose, 4.9% by weight extra-granular sodium croscarmellose, 11.6% by weight extra-granular sodium croscarmellose, 0.5% by weight colloidal silicon dioxide (Cab-O-Sil™ M-5), and 1.5% by weight magnesium stearate powder.

In another preferred first embodiment, the abridged compositions are substantially bioequivalent to the non-abridged formulations.

In still another preferred first embodiment, the abridged compositions are for oral administration in tablet form, such as, for example, tablets which weigh 750 mg.

These preferred embodiments may combine to provide an abridged antibacterial composition for the oral administration of clarithromycin in tablet form, the tablet weighing 750 mg and consisting essentially of 250 mg of clarithromycin, water, an intra-granular excipient, and an extra-granular excipient,

in which the granular excipient consists essentially of

4.9% by weight povidone, 4.9% by weight sodium croscarmellose, and microcrystalline celluose (Avicel® PH-101), and

the extra-granular excipient consists essentially of 4.9% by weight sodium croscarmellose, 11.6% by weight microcrystalline celluose (Avicel® PH-102), 0.5% by weight colloidal silicon dioxide (Cab-O-Sil M-5), and 1.5% by weight impalpable magnesium stearate powder; and

an abridged antibacterial composition for oral administration of clarithromycin in tablet form, the tablet weighing 750 mg and consisting essentially of 500 mg of clarithromycin, water, an intra-granular excipient, and an extra-granular excipient, in which the granular excipient consists essentially of

4.9% by weight povidone, 4.9% by weight sodium croscarmellose, and microcrystalline celluose (Avicel® PH-101), and

the extra-granular excipient consists essentially of 4.9% by weight sodium croscarmellose, 11.6% by weight microcrystalline celluose (Avicel® PH-102), 0.5% by weight colloidal silicon dioxide (Cab-O-Sil M-5), and 1.5% by weight impalpable magnesium stearate powder.

In a preferred second embodiment, the microcrystalline celluose of the intra-granular excipient comprises Avicel® PH-101, the microcrystalline celluose of the extra-granular excipient comprises Avicel® PH-102, and the colloidal silicon dioxide of the extra-granular excipient comprises Cab-O-Sil M-5.

In another preferred second embodiment, the process further comprises adding a solution of povidone in water to the material to be granulated in step (a), in which the amount of water is present in 39% by weight to 44% by weight of the material to be granulated.

In a preferred third or fourth embodiment, the medicament is a 750 mg tablet containing 250 mg clarithromycin, an intra-granular excipient, and an extra-granular excipient.

In another preferred third or fourth embodiment, the medicament is a 750 mg tablet containing 500 mg clarithromycin, an intra-granular excipient, and an extra-granular excipient.

The following bioequivalence study was conducted at Sea View Research, Inc. (Miami, FL).

Fifty-six (56) healthy adult male and female subjects were enrolled in the study. Fifty-four (54) subjects completed all four periods of the study. Subject 6 received only one dose of study drug and was terminated from the study due to a positive drug screen. Subject 45 received three doses of the study drug and was terminated from the study due to adverse events. Neither of the terminated subjects had complete data for the reference formulation under nonfasting or fasting conditions. For the 54 subjects (36 males and 18 females) who completed the study, nine were Caucasian, three were Black, and 42 were Hispanic. The mean age was 34.4 years (range: 19 to 49 years), the mean weight was 71.4 kg (range: 52 to 89.5 kg) and the mean height was 167.2 cm (range: 149 to 196 cm).

DRUG FORMULATIONS

Formulation A: test clarithromycin 500 mg tablet formulation manufactured by Abbott Laboratories (Abbott Park, IL).

Formulation B: reference (BIAXIN®) clarithromycin 500 mg tablet formulation manufactured by Abbott Health Products Inc. (Barceloneta, Puerto Rico).

STUDY DESIGN AND DOSE ADMINISTRATION

This was a Phase I, single-dose, open-label, randomized, four-period, complete-crossover study. Regimen A was defined as one tablet of Formulation A (test) administered approximately 30 minutes after the start of breakfast. Regimen B was defined as one tablet of Formulation A (test) administered after an eight-hour fast. Regimen C was defined as one tablet of Formulation B (reference) administered approximately 30 minutes after the start of breakfast. Regimen D was defined as one tablet of Formulation B (reference) administered after an eight-hour fast.

SAMPLE COLLECTION

Blood samples (7 mL) were collected into heparinized evacuated collection tubes prior to dosing (0 hour) and at 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 10, 12, 15, 18 and 24 hours after dosing in each study period.

ANALYTICAL METHODOLOGY

Plasma samples were analyzed for clarithromycin at BAS Analytics (West Lafayette, Indiana) using a validated HPLC procedure. The lower limit of quantification was 0.0156 μg/mL. The assays were conducted from December 19, 1997 through January 28, 1998.

PHARMACOKINETIC ANALYSES

Pharmacokinetic parameter values were estimated for clarithromycin using noncompartmental methods. The pharmacokinetic parameters included maximum observed plasma concentration (C_{max}), the time of C_{max} (T_{max}), the area under the plasma concentration-time curve from time 0 to the time of the last measurable plasma concentration ($AUC_{0\text{-}last}$), the AUC extrapolated to infinite time ($AUC_{0\text{-}\infty}$), the terminal elimination rate constant (β) and the half-life ($t_{1/2}$).

STATISTICAL ANALYSES

Analyses of variance (ANOVAs) were also performed for T_{max} (hours) and the natural logarithms of C_{max} (μg/mL), $AUC_{0\text{-}last}$ (μg·h/mL), and $AUC_{0\text{-}\infty}$ (μg·h/mL). The model included effects for sequence, subject nested within sequence, and period and regimen. Within the ANOVA modeling framework, the test formulation under fasting conditions (Regimen B) was compared to the reference formulation under fasting conditions (Regimen D), the test formulation under nonfasting conditions (Regimen A) was compared to the reference formulation under nonfasting conditions (Regimen C), and the test formulation under nonfasting conditions (Regimen A) was compared to the test formulation under fasting conditions (Regimen B), each with an alpha level of 0.05.

Within the framework of the ANOVA's for the logarithms of C_{max} and AUC, the bioavailability of the test formulation under fasting conditions (Regimen B) relative to the reference formulation under fasting conditions (Regimen D) was assessed by the two one-sided tests procedure *via* 90% confidence intervals. The confidence interval for relative bioavailability was obtained by exponentiating the endpoints of a confidence interval for the difference of logarithm means. Similarly, the bioavailability of the test formulation

under nonfasting conditions (Regimen A) relative to that of the test formulation under fasting conditions (Regimen B) was assessed *via* 95% confidence intervals.

RESULTS

Summaries (mean ± standard deviation) of the pharmacokinetic parameter estimates for clarithromycin are presented hereinbelow.

Regimen	C_{max}	T_{max}	$AUC_{0\text{-last}}$	$AUC_{0\text{-}\infty}$	$t_{1/2}$*
A	2.98±1.12[b,c]	2.5±1.0[c]	16.8±6.0	17.3±6.2	4.3
B	2.38±0.86	1.9±0.8[a]	16.3±5.0	17.8±6.8	4.3
C	2.65±1.17	2.4±0.6	2.4±6.5	16.1±6.6	4.3
D	2.39±0.98	2.4±2.1	16.9±6.0	17.6±6.1	4.7

[a]Significantly different ($p<0.05$) from reference formulation under fasting conditions (Regimen D).

[b]Significantly different ($p<0.05$) from reference formulation under nonfasting conditions (Regimen C).

[c]Significantly different ($p<0.05$) from test formulation under fasting conditions (Regimen B).

*Half-life is presented as the harmonic mean; this parameter was not subjected to statistical analysis.

These data illustrate the bioequivalence of the abridged and non-abridged 500 mg clarithromycin formulations.

The following will provide a better understanding of the compositions and processes of this invention.

Both microcrystalline celluloses were purchased from FMC BioPolymer (Cork, Ireland); Magnesium Stearate was purchased from Mallinckrodt-Baker, Inc (ST Louis, Mo); Collodial silicon dioxide was purchased from Cabot Corp. (Tuscola, IL); povidone was purchased from ISP Technologies (Texas City, TX); sodium croscarmellose was purchased from Noviant (Nijmegan, Netherlands); or from FMC BioPolymer (Newark, DE).

GRANULATION

Povidone (K-value Range 29-32, 125.80 kg) was dissolved in purified water (1384.89 kg) to prepare an approximately 8.33% w/w solution.

Clarithromycin bulk drug (1360.00 kg), sodium croscarmellose (100.64 kg), and microcrystalline cellulose, (PH-101, 100.64 kg) were charged into a high intensity 1200L Gral masser bowl, mixed for 5 minutes on low speed (chopper off), treated with the 8.33% w/w povidone in water (0.774 kg of solution per kg of material to be granulated) at the rate of 30 kg per minute at low speed (chopper and mixer), and granulated on high speed (chopper and mixer) for 4 minutes (9 minutes total granulation time).

A power increase from the baseline was determined, and if the significant power increase was observed, the next step was conducted immediately. If a significant power increase was not observed, further granulation was conducted using additional purified water. When significant power increase was attained, the mixture was granulated for one additional minute (chopper and mixer on high).

The contents of the high intensity masser were discharged into a fluid bed dryer bowl and dried to provide a loss on drying of not more than 0.8% using a gravimetric moisture tester. The bowl of wet granulation was positioned in an Aeromatic Dryer, and the filter bag was shaken manually, as needed, to keep most of the granulation in the dryer bowl. A shock cycle and/or agitator was used as needed to fluidize any stationary material.

The bowl was removed from the fluid bed dryer, and its contents were discharged, with an inverter cone-attached, into an impact mill, granulation mill dried through a 2AA band (or 14 mesh screen) at medium speed with knives forward, and discharged into appropriate containers.

LUBRICATION

Approximately one-half of the granulation was charged into a V-blender followed by sodium croscarmellase (100.64 kg), microcrystalline cellulose (PH-102, 236.64 kg), magnesium stearate (29.92 kg), and colloidal silicon dioxide (10.88 kg) through a 30 mesh screen using a speed sifter, followed by transfer of the remainder of the granulation, and blended for at least 30 minutes using a 150 cubic foot V-blender or for at least 20 minutes

using a 75 cubic foot V-blender, and discharged into appropriate containers. Room RH control must not be more than 25% (or low setting) during this step.

COMPRESSING

The tablets were compressed using a rotary tablet compressing machine installed with ovaloid lower punch with Abbo Code KL and ovaloid upper punch with Abbott Corporate Logo. A de-duster was employed, as necessary. The theoretical weight of 10 tablets was 7.50g.

COLOR COATING LIQUID MANUFACTURE

A color coating liquid was prepared by adding a portion of purified water (792.82L) into the mix tank, mixing at high speed while reducing speed, as necessary to minimize foaming, treating the mixture with Opadry Yellow® (YS-5-12749, 85.65 kg) and propylene glycol (21.63 kg), mixing until all solid dissolved, and mixing the coating liquid at least one hour prior to sampling.

The tablets were coated with 400 mL of color coating liquid per kg weight of uncoated tablets using an Accela-Cota or equivalent size vented perforated pan coater. The target run size for 60" pan coater is approximately 245 kg. Mixers were used to maintain motion in the liquids to keep the solids suspended. A distance between the nozzles and tablet bed was maintained while running. These parameters are summarized in TABLE 1 below.

TABLE 1

Parameter	Set Point	Range (±)	Unit of Measure
Air Supply Upper Limit Temperature for Color	95	N/A	°C
Exhaust Air Temperature for Color Application	48	5	°C
Supply Air Rate	4000	N/A	SCFM
Liquid Flow Rate, Volume, Color	0.65	0.2	Kg/min
Atomization Pressure for Color	80	5	PSIG

Pan Speed	6	2	RPM
Distance Between Nozzles and Tablet Bed, Color	9	1	Inches

The foregoing is merely illustrative of the invention and is not intended to limit the same to the disclosed compounds and processes. Variations and changes which are obvious to one skilled in the art, as defined in the claims, are intended to be within the scope and nature of the invention.

WHAT IS CLAIMED IS:

1. An abridged antibacterial composition consisting essentially of clarithromycin, water, an intra-granular excipient, and an extra-granular excipient, in which the intra-granular excipient consists essentially of povidone, sodium croscarmellose, and microcrystalline celluose, and the extra-granular excipient consists essentially of sodium croscarmellose, microcrystalline celluose, colloidal silicon dioxide, and impalpable magnesium stearate powder.

2. The composition of claim 1 in which the microcrystalline celluose of the intra-granular excipient comprises Avicel® PH-101, the microcrystalline celluose of the extra-granular excipient comprises Avicel® PH-102, and the colloidal silicon dioxide of the extra-granular excipient comprises Cab-O-Sil™ M-5.

3. The composition of claim 1 which is essentially ethanol-free.

4. The composition of claim 2 which is an immediate-release composition for oral administration.

5. The composition of claim 4 which, when ingested orally, has a substantially equivalent pharmacokinetic profile as the non-abridged composition.

6. The composition of claim 4 which, when ingested orally, has a substantially improved pharmacokinetic profile as the non-abridged composition.

7. The composition of claim 4 or claim 5 in tablet form, in which the tablet weighs 750 mg and consists essentially of 250 mg of clarithromycin.

8. The composition of claim 4 or claim 5 in tablet form, in which the tablet weighs 750 mg and consists essentially of 500 mg of clarithromycin.

9. The composition of claim 3, 4, 5, 6, 7, or 8 in which the povidone is present in 4.0% to 5.9% by weight, the intra-granular sodium croscarmellose is present in 3.0% to 6.8% by weight, the intra-granular microcrystalline celluose is

present in 2.2% to 7.5% by weight, the extra-granular sodium croscarmellose is present in 3.0% to 6.8% by weight, the extra-granular microcrystalline celluose is present in 6.9% to 15.9% by weight, the colloidal silicon dioxide is present in 0.5% to 0.8% by weight, and the magnesium stearate powder is present in 1.5% to 2.5% by weight.

10. The composition of claim 9 in which the povidone is present in 4.9% by weight.

11. The composition of claim 9 in which the intra-granular sodium croscarmellose is present in 4.9% by weight.

12. The composition of claim 9 in which the extra-granular sodium croscarmellose is present in 4.9% by weight.

13. The composition of claim 9 in which the extra-granular sodium croscarmellose is present in 11.6% by weight.

14. The composition of claim 9 in which the silicon dioxide is present in 0.5% by weight.

15. The composition of claim 9 in which the magnesium stearate is present in 1.5% by weight.

16. An abridged antibacterial composition for the oral administration of clarithromycin in tablet form, the tablet weighing 750 mg and consisting essentially of 250 mg of clarithromycin, water, an intra-granular excipient, and an extra-granular excipient, in which the intra-granular excipient consists essentially of 4.9% by weight povidone, 4.9% by weight sodium croscarmellose, and microcrystalline celluose (Avicel® PH-101), and the extra-granular excipient consists essentially of 4.9% by weight sodium croscarmellose, 11.6% by weight microcrystalline celluose (Avicel® PH-102), 0.5% by weight colloidal silicon dioxide (Cab-O-Sil™ M-5), and 1.5% by weight impalpable magnesium stearate powder.

17. An abridged antibacterial composition for oral administration of clarithromycin in tablet form, the tablet weighing 750 mg and consisting essentially of 500 mg of clarithromycin, water, an intra-granular excipient, and an extra-granular excipient, in which the intra-granular excipient consists essentially of 4.9% by weight povidone, 4.9% by weight sodium croscarmellose, and microcrystalline celluose (Avicel® PH-101), and the extra-granular excipient consists essentially of 4.9% by weight sodium croscarmellose, 11.6% by weight microcrystalline celluose (Avicel® PH-102), 0.5% by weight colloidal silicon dioxide (Cab-O-Sil™ M-5), and 1.5% by weight impalpable magnesium stearate powder.

18. A process for making an abridged antibacterial clarithromycin composition, the process comprising the steps of:

(a) granulating a mixture consisting essentially of povidone, clarithromycin, sodium croscarmellose, microcrystalline celluose, and water to provide a wet intra-granular excipient;

(b) drying the wet intra-granular excipient to provide a dry intra-granular excipient; and

(c) mixing the dry intra-granular excipient and an extra-granular excipient, the extra-granular excipient consisting essentially of sodium croscarmellose, microcrystalline celluose, colloidal silicon dioxide, and impalpable magnesium stearate powder.

19. The composition of claim 1 in which the microcrystalline celluose of the intra-granular excipient comprises Avicel® PH-101, the microcrystalline celluose of the extra-granular excipient comprises Avicel® PH-102, and the colloidal silicon dioxide of the extra-granular excipient comprises Cab-O-Sil™ M-5.

20. The process of claim 18 further comprising adding a solution of povidone in water to the material to be granulated in step (a).

21. The process of claim 20 in which the amount of water is present in 39% by weight to 44% by weight of the material to be granulated.

22. Use of the abridged antibacterial clarithromycin composition of any of claims 1 to 17 and 19 in the preparation of a medicament, the medicament being useful for prophylaxis or treatment of bacterial infections in a mammal.

23. Use of the abridged antibacterial clarithromycin composition of any of claims 1 and 16 in the preparation of a medicament, in which the medicament is a 750 mg tablet containing 250 mg of clarithromycin.

24. Use of the abridged antibacterial clarithromycin composition of any of claims 1 and 17 in the preparation of a medicament, in which the medicament is a 750 mg tablet containing 500 mg of clarithromycin.

25. A medicament consisting essentially of the abridged antibacterial clarithromycin composition of any of claims 1 and 16, wherein the medicament is a 750 mg tablet containing 250 mg of clarithromycin, an intra granular excipient, and an extra granular excipient.

26. A medicament consisting essentially of the abridged antibacterial clarithromycin composition of any of claims 1 and 17, wherein the medicament is a 750 mg tablet containing 500 mg of clarithromycin, an intra granular excipient, and an extra granular excipient.

27. Use of the abridged antibacterial clarithromycin composition as defined in any of claims 1 to 17 and claim 19 in the prophylaxis or treatment of bacterial infections in a mammal.

28. Use of the abridged antibacterial clarithromycin composition made by the process defined in any of claims 18, 20 and 21 in the prophylaxis or treatment of bacterial infections in a mammal.